REMARKS

The Final Office Action mailed October 23, 2008 has been carefully reviewed and the following remarks are made in response thereto. Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Claims 11-12, 17-67 are pending. As a result of restriction and elections, claims 17-20 and 32-66 have been withdrawn.

I. Summary of the Office Action

1. Claims 11-12 and 17-67 will be pending upon entry of the attached amendment.

2. The Examiner rejected claims 11-12, 21-22, 30-31, and 67 under 35 U.S.C. 103(a) as being anticipated by Vande-Velde, U.S. PG Patent No. 20040013695, in view of Zanone *et al.*, U.S. Patent No. 6,497,859.

3. The Examiner rejected claims 23-25 under 35 U.S.C. 103(a) as allegedly being unpatentable over Vande-Velde and Zanone *et al.*, as applied to claims to claims 11-12 and 21-22, in view of Martin *et al.*, U.S. PG Patent No. 20030049271.

4. The Examiner rejected claims 23 and 26-29 under 35 U.S.C. 103(a) as allegedly being unpatentable over Vande-Velde and Zanone *et al.*, as applied to claims 11-12 and 21-22, in view of Kricek, *et al.*, U.S. Patent No. 6,610,297.

5. The Examiner rejected claims 11-12 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,348,010, in view of Vande-Velde and Zanone *et al.*

6. The Examiner provisionally rejected claims 11-16 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 63-64 of copending Application No. 10/490,920 in view of Vande-Velde and Zanone *et al.*

7. No claims were allowed.

II. Response to the Office Action

1. Claim Rejection under § 103

The Examiner rejected claims 11-12, 21-22, 30-31, and 67 under 35 U.S.C. 103(a) as being anticipated by Vande-Velde, U.S. PG Patent No. 2004/0013695, in view of Zanone *et al.*, U.S. Patent No. 6,497,859. The Examiner contends that Vande-Velde teaches an oral vaccine composition comprising an antigenically active substance and an antacid for dissolution in the mouth. The Examiner acknowledges that it is not apparent whether the antacids disclosed in Vande-Velde act protectively through mucous membranes. However, the Examiner cites Zanone et al., for the teaching that numerous compounds, including those taught by Vande-Velde and those mentioned in the present application, can be used as antacids. Therefore, the Examiner reasons that it would have been obvious to use an antacid disclosed by Zanone et al., which include those of the present invention, with the composition of Vande-Velde, because the use of functional equivalents, i.e., one antacid for another, is routinely practiced in the art.

Applicants respectfully traverse the rejection. As previously mentioned, the antacids described in Vande-Velde are limited to antacids that perform a neutralization reaction to reduce acidity in the stomach. Specifically Vande-Velde at paragraph [0006] states:

> In another aspect of the present invention the oral vaccine quick dissolving cake comprises an antacid. The antacid being such that when dissolved in saliva, and swallowed, it is capable of raising the pH of the stomach contents such that the vaccine antigen is not substantially degraded in the stomach. Most preferably the antacid is water insoluble and also acts as an adjuvant, in addition it is more preferred that when antigen is adsorbed to the surface of the insoluble antacid/adjuvant the antigen is protected from stomach acid.

The primary purpose of the antacids of Vande-Velde are to raise the pH of the stomach to avoid degradation of the proteinaceous antigens. Vande-Velde does not teach the currently recited class of antacids, namely antacids that act protectively through the mucous membrane.

Antacids that act protectively through the mucous membrane, such as sucralfate and carbenoxolone (paragraph [0016], [0035]), are characterized by a different mode of action than those disclosed by Vande-Velde. For example, sucralafte is a locally-acting substance that, when in an acidic environment (pH <4), binds to hydrochloric acid of the stomach to form a cross-

linking, viscous, paste-like material capable of acting as an antacid buffer that protects the mucosa from endogenous and exogenous noxious agents for as long as six to eight hours after a single dose. These cytoprotective properties result from a locally-formed layer that covers ulcers and erosions which inhibits the diffusion of protons and pepsin to the damaged mucosa. ***Unlike the antacids of Vande-Velde, there is no influence of sucralfate on the production of gastric juice and gastric pH.*** Sucralfate attaches to the proteins on an ulcer surface, such as albumin and fibrinogen, to form stable insoluble complexes. These complexes serve as protective barriers at the ulcer surface, thereby preventing further damages from acids, peptides, and bile. Sucralfate also absorbs both peptide and bile acids. Accordingly, Vande-Velde does not teach antacids that act protectively through the mucous membrane.

Moreover, there is an unexpected increase of vaccine immunogenicity when using antacids that protectively act through the mucous membrane. The instantly claimed composition provides for a vaccine that generates an improved immune response involving the production of immunoglobulins. The response is a Type 2 immune response which involves the generation of IgE. See paragraphs [0006-0007]. Vande-Velde do not teach or suggest that antacids can be used to stimulate a Type 2 immune response. In fact, the examples of Vande-Velde, teach away from the instant invention because the data show that the oral formulations comprising antacids disclosed by Vande-Velde actually elicit a **lower** immune response than corresponding intramuscular injections. See paragraph [0069] ("In general, the oral lyoc formulations elicited lower serum IgG responses than the OspA IM booster."). In contrast, the data in Figure 1 of the instant application shows an unexpectedly **higher** immunogenic response when using sucralfate, for example, as compared to a corresponding intramuscular injection. In Example 1, the present invention demonstrates that the immune response is improved by using an antacid that acts protectively through the mucous membrane versus the antacids disclosed by Vande-Velde. See Group B versus Group C.

The Examiner's citation to Zanone *et al.* to simply show that sucralfate is an antacid does not cure the deficiencies of Vande-Velde. Zanone *et al.* is generally directed to the use of cooling agents which include, among others, sucralfate, for treating inflammatory irritations of the upper gastric tract. Nowhere do Zanone *et al.* teach or suggest that antacids can be used to

induce or increase an immune response. Moreover, Zanone *et al.* do not distinguish the immunological response differences between the instantly claimed antacid and the antacids disclosed by Vande-Velde.

Viewing the prior art as a whole, a person of ordinary skill in the art would not have been motivated to combine the teachings of Vande-Velde and Zanone *et al.* Vande-Velde teaches the combination of an oral vaccine comprising an antigen and an antacid does not lead to an improved immune response and neither reference discloses an increased immune response when using the currently recited antacid species. Accordingly, a person of ordinary skill in the art would not have a reasonable expectation of success to combine these references. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

The Examiner rejected claims 23-25 under 35 U.S.C. 103(a) as allegedly being unpatentable over Vande-Velde and Zanone *et al.*, as applied to claims to claims 11-12 and 21-22, in view of Martin *et al.*, U.S. PG Patent No. 20030049271. The Examiner also rejected claims 23 and 26-29 under 35 U.S.C. 103(a) as allegedly being unpatentable over Vande-Velde and Zanone *et al.*, as applied to claims 11-12 and 21-22, in view of Kricek, *et al.*, U.S. Patent No. 6,610,297. Applicants respectfully traverse these rejections.

As discussed above, a person of ordinary skill would not have had a reasonable expectation of success of an improved immune response using the claimed antacid species. Neither Martin *et al.* nor Kricek *et al.* remedy the insufficiency of the Examiner's initial obviousness rejection. Martin *et al.* is generally directed to *Streptococcus* antigens and do not teach or suggest degeneration by stomach acids, the use of the claimed antacid, or an increased immune response when using the same. Similarly, Kricek *et al.* do not teach or suggest degeneration by stomach acids, the use of the claimed antacid, or an increased immune response when using the same. For these reasons, withdrawal of these rejections under 35 U.S.C. § 103(a) is respectfully requested.

2. Double Patenting

The Examiner rejected claims 11-12 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,348,010, in view of

Vande-Velde and Zanone *et al.* The Examiner also provisionally rejected claims 11-16 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 63-64 of copending Application No. 10/490,920 in view of Vande-Velde and Zanone *et al.* Applicants respectfully traverse these rejections.

As discussed above, a person of ordinary skill would not have a reasonable expectation of success of an improved immune response using the claimed antacid species. Neither U.S. Patent No. 7,348,010 nor U.S. Application No. 10/490,920 cure the deficiency of the Examiner's initial obviousness rejection as neither teach or suggest degeneration by stomach acids, the use of the claimed antacid, or an increased immune response when using the same. For these reasons, withdrawal of these rejections under non-statutory obviousness-type double patenting is respectfully requested.

III. Conclusion

Applicant believes that the above-referenced application is in condition for allowance. Reconsideration and withdrawal of the outstanding rejections and early notice of allowance to that effect is respectfully requested.

> **EXCEPT** for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 13-3250, reference No. 37488.00400. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

If the Examiner finds that a telephone conference would further prosecution of this application, the Examiner is invited to contact the undersigned at 202-835-7589.

Respectfully submitted,

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Dated: January 22, 2009

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